Evaluating Cost Effectiveness Models

Part 10

Decision Rules, Economic Evaluation and Decision-Making in the Real World

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Presentation Outline

- Decision rules for economic evaluations
- Worldwide experience
  - Specific Issues
  - Economic Modeling
- US environment
- Two examples

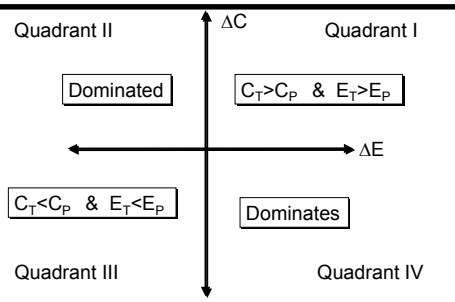
CEA for decision making

- Definition:
  - A formal method for comparing the cost and benefits of a medical intervention in order to determine whether it is of sufficient value to adopt or reimburse.
  - Costs are measured in physical units and valued in monetary units.
  - Effectiveness is measured in natural units of health improvement - clinical outcome measure, years of added life, prevention of event.
- Model:
  - $[\{C_{int1} + C_{care1} + C_{se1} + C_{am1}\} - \{C_{int2} + C_{care2} + C_{se2} + C_{am2}\}] / [E_1 - E_2]$

The CEA Ratio

- Issues with the CEA ratio:
  - Double-counting. The US panel recommends that the denominator be free from cost measures. Ratios that display "cost per event-avoided" should be avoided because of double counting.
  - Comparability. Cost/QALY is not always feasible or relevant for health care interventions. For resource allocation decision rules to apply, CEA studies must be standardized (Gold et al 1997).
    - Methods
    - Endpoint selection
    - Time horizon
  - Uncertainty. Failure to consider interdependence (covariance) of costs and benefits leads to bias in CI estimation.

Interpretation of CEA results



League Tables

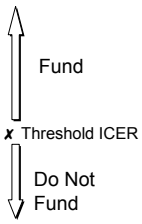
Intervention	Incremental CER
A	$25,000/QALY
B	$33,000/QALY
C	$35,000/QALY
D	$40,000/QALY
E	$60,000/QALY

Resource allocation decision rules for CEA

- Absolute Budget Constraint Rule:
  - Implement interventions, starting with the most cost-effective alternatives, until health care budget is exhausted.
    - The Oregon Medicaid experiment.
- Relative Budget Constraint Rule:
  - Implement all interventions that fall below a stated threshold (budget constraint) ICER.

Budget Constraint Application

Intervention	Incremental CER
A	$25,000/QALY
B	$33,000/QALY
C	$35,000/QALY
D	$40,000/QALY
E	$60,000/QALY



Limitations of league tables

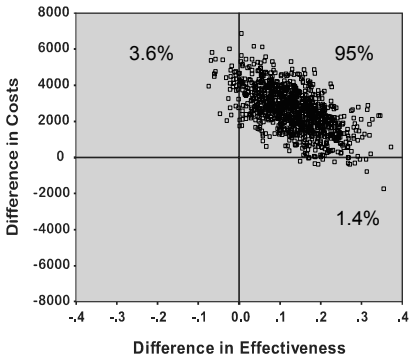
- Methods and measurements:
  - All resources measured and valued.
  - Perspective and discount rate used.
  - Measurement of utility.
  - Relevant comparator.
  - The impact of uncertainty on point estimates of ICER.

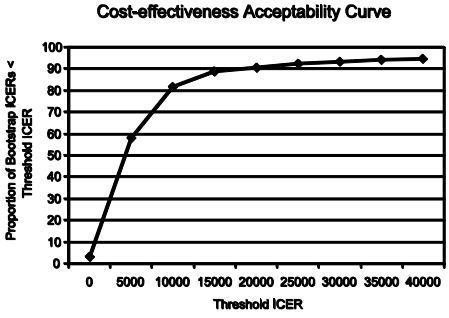
Limitations of the decision rules

- Implementation for decision making
  - Under the "relative" rule, a decision-maker could exhaust resources on cost-effective therapies. There is no absolute financial constraint.
  - Under the "absolute" rule, some interventions judged to be cost-effective would not be funded.
  - If an equal cost-effectiveness ratio (i.e., same cost/QALY) was achieved for two drugs in different therapeutic categories, a budget impact analysis would show a preference for the drug used to treat a disease with a lower prevalence, since this would lead to lower expenditures, all other things equal.

Point estimates and confidence limits: budget constraint of $50,000

Intervention	Incremental CER	95% CI	
A	$25,000/QALY	$23,000 - $27,000	✓
B	$33,000/QALY	$25,000 - $65,000	?
C	$35,000/QALY	$31,000 - $37,000	✓
D	$40,000/QALY	$30,000 - $50,000	✓
E	$60,000/QALY	$35,000 - $95,000	?





Conclusions

- Which method is most appropriate for decision-making?
  - There is no universal support for any one method, though most decision-makers prefer comparative methods.
  - The results and interpretation of these evaluations are subject to the limitations of the science.
- There is no evidence that health plans or government agencies worldwide make medical care payment decisions strictly on rules of economic efficiency.
  - The PBAC and other bodies subscribe to a multifactorial model of decision making. Economic appraisal plays a somewhat limited role.

Background: Drug Expenditure Trends

- Age-adjusted average expenditures for prescription drugs rose 24.8% per year between 1996 and 1999.

  – RxHealth Value Center, Brandeis University; May 2000

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Background: Drug Expenditure Trends

- Contributing factors to drug expenditure escalation:
  - Increase in prescriptions per user - **38.4%**
  - Increase in duration of prescription - **19.0%**
  - Substitution of newer, more expensive drugs for existing drug therapy - **17.2%**
  - New users, previously untreated - **14.0%**
  - Increase in price - **4.4%**
  - Combination of price/quantity - **7.0%**

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Background

- Expenditure trends strongly suggests:
  - The process for selecting and managing the use of pharmaceuticals by health plans needs to be improved.
  - Health plans need to employ rigorous technology assessment programs in order to evaluate the evidence of benefit, safety and value of new compounds.

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Background

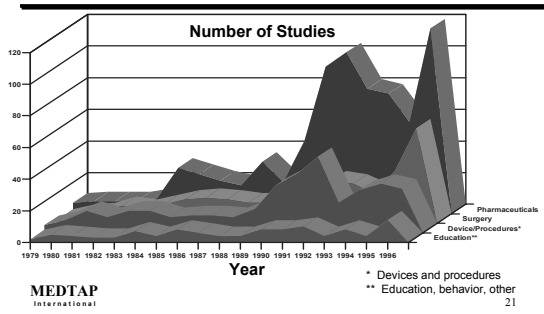
- Health Authorities and Organizations With Comprehensive Tech Assessment Programs.
  - 1991 - Australia Pharmaceutical Benefits Advisory Committee (PBAC)
  - 1994 - Canada (CCOHTA)- Province-specific requirements
  - 1999 - UK - National Institute Clinical Excellence (NICE)
  - EU - 7+ Countries
  - Blue Cross and Blue Shield Association (TEC)
  - BCBS RxIntelligence
  - HCFA Proposed "Criteria for making coverage decisions."
  - 2000 - AMCP

The European Experience

	Reimbursement decisions	Price Negotiations	Local formulary decisions	Developing clinical guidelines	Communications to prescribers
Belgium	*		*		*
Denmark	*		*	*	
Finland	*	*		*	
France	*	*			
Germany			*	*	*
Italy	*				
Netherlands	*		*	*	*
Norway	*	*			*
Portugal	*				*
Spain	*				
Sweden	*	*	*	*	*
Switzerland	*	*			
U.K.			*	*	*
U.S.			*		Sec 114

Adapted from Drummond et al 1999 Value in Health.

Frequency of Economic Impact Studies



MEDTAP International

* Devices and procedures
** Education, behavior, other

Communicating Information: Four Legal Authorities

- Scientific Communications
- General Audience/Media (FDA Law)
- Formulary Committees (FDAMA)
- Unsolicited Requests**

MEDTAP International

Unsolicited Requests

- Role of the FDA is limited to assuring that these requests are truly unsolicited.
- Communication can exist between the pharmaceutical industry and the health plans.
  - off-label information
  - outcomes information
  - database studies
  - health economics and modeling studies

Unsolicited Requests

The AMCP guidelines provide a standardized template for a broad unsolicited request for all product-related information, some of which are not currently available to health plans.

Background

- Manufacturers would like increased access to the formulary process
  - Formularies and the formulary approval process have been criticized by the pharmaceutical industry as lacking scientific basis
  - Regulatory restrictions imposed by FDA on communication of health economics information.
  - To make the value argument about their products
- AMCP and member plans have an interest in:
  - Improved formulary decision making
  - Appropriately using outcomes and economics data in the formulary process

Motivation

- Recognize the need for combining efficacy, safety, effectiveness, and economic evaluation for the formulary decision-making process
- Provide a consistent and direct means for the manufacturer to supply information directly to the health plan in order to support use of the agent

Motivation

- Emphasize that simple acquisition cost reduction **is not** be the most cost-efficient approach to controlling overall health care expenditures

AMCP Guidelines: Goals

- Advocating a comprehensive, standardized, evidence-based process for the submission of clinical and economic data to health plans.
- Providing manufacturers with a consistent format for providing necessary information.
- Improving the transparency and relevance of the available clinical, outcomes and economic data to pharmacy staff and P/T committee.

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AMCP Guidelines: Content

- Overview and role of guidelines in the health plan
- Instructions for Submission
- Content of the Submission Document
  - Disease Description and Agent's Role in Therapy
  - Clinical Efficacy, Safety, and Effectiveness
  - Economic Evaluations
  - Modeling
- Value Justification
- Supporting Information

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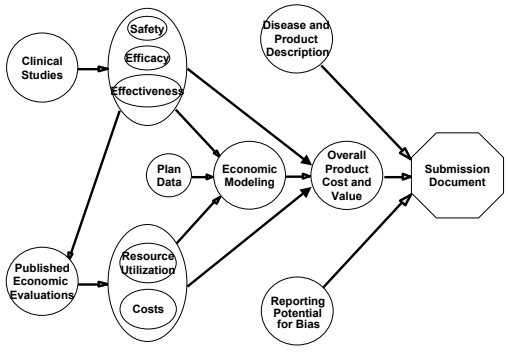

AMCP Guidelines: Specific Issues

- Submission:
  - Will it be required for each product? Line extensions (e.g. Prozac q weekly?)
  - Does not guarantee formulary approval
- The AMCP guidelines do not specify methods for economic evaluation. It is the submitter's responsibility to utilize appropriate techniques and data sources.
- Justifying the price of a new agent in terms of its health value to the health plan.

AMCP Guidelines: Economic Evaluations

- Requirements:
  - Disease-based models only - no RCT-specific models
  - Broadly applicable to the health plan population
    - Models developed for other purposes are OK
  - Address the system-wide impact of formulary changes on:
    - Clinical outcomes
    - Resource utilization and costs
  - Transparent presentation of results

AMCP Guidelines: Models

- Economic Models:
  - An analytic structure for presenting an evaluation of the potential impact of a drug on the costs and outcomes of care:
    - Using data from trials, databases, literature and other sources;
    - Comparing new drug to currently used alternatives;
    - Within a usual care clinical framework of relevance to the health plan;
    - Considering the costs that the health plan faces.
  - These 'models' are typically presented in a spreadsheet format.

Checklist for Good Models

- Structure:
  - Is it a disease-progression model with appropriate time horizon?
  - Are the treatment pathways relevant to the decision?
  - Does it model usual clinical practice?
  - Is the model calibrated to population-based evidence?
  - Are the mathematics of the model accurate and available for inspection?

Checklist for Good Models

- Data:
  - Are the sources of evidence valid?
  - Have the data been interpreted and incorporated accurately?
  - Have uncertainties in the data been addressed?
  - Are linkages between intermediate and long-term outcomes:
    - Valid (Face and External)?
    - Based on appropriate (trial or retrospective) evidence?

Checklist for Good Models

- Outputs
  - Outcomes relevant to decision-making in the health plan?
  - Incremental analyses performed on both health effects and costs?
  - Verifiable? Traceable back to the inputs and model structure.
  - Uncertainty in the data tested in a reasonable fashion.
  - Results and uncertainty presented in a fashion that facilitates incorporation into formulary monographs and decision-making?

Issues to Consider

- What are the requirements of the formulary committee for economic data?
  - Budget impact model (drug budget, total cost?)
  - Cost-consequence or balance sheet model
  - Cost-effectiveness model
- What is the perspective of the formulary committee?
  - Societal perspective often makes no sense.
- Disease progression vs. clinical trial-based model?
- Statistical significance vs. financial significance?

Recommendations

But . . .

Perfection is the enemy of the good.

2 Examples of AMCP Submissions

Statin Class

- HMG CoA Reductase Inhibitors
  - All medications in this class inhibit an enzyme that is the rate limiting step in cholesterol synthesis.
  - Statins represent the third largest RX sales volume in the US as a class.
  - 3 of the top 10 drugs (by expenditure) are statins.
  - 1999 - RBS paid $6.73 million for statin medications.

Statin Class

- Issues for the plan
  - 6 medications in the class
  - Range in price from $45 to $120 per month.
  - MFRs optimize rebates if the health plan has a formulary with 3 or fewer agents.

Statin Class

- Questions for P&T
  - Are all six of these products equivalent in terms of long-term outcomes and costs?
  - When choices can be made, should the P&T committee reward companies for conducting long-term outcomes studies?
  - Will reducing the number of available products from 6 to 3 reduce access and harm quality of care?
  - Can RBS take advantage of the MFRs designated rebates?

Clinical review of the statins

- All statins show a significant dose response in lowering LDL (bad).
- All statins increase HDL (good).
- The statins have variable potency.
- Several large RCTs have shown significant reductions in cardiovascular mortality.
- JAMA article described the cardiovascular outcomes of statin therapy as being uniform.

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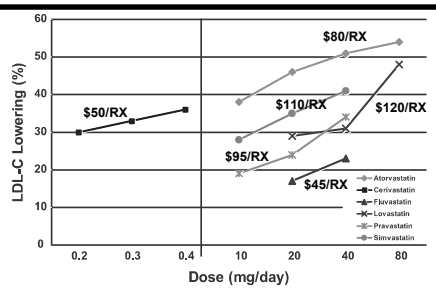
Efficacy and Cost of Statins



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Decision on HMG-CoA

- Statins are effective and cost- effective as primary and secondary prevention.
- Declare that the clinical utility of more than three agents is marginally small.
- Reward companies that invest in health outcomes evaluations.

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Statin Market Share and Cost Scenarios to mid-2000

Formulary Status	Lipitor	Lescol	Pravachol	Baycol	Zocor	Mevacor	Projected Annual Cost
Base Case	59	7	22	2	9	2	$6.730
B-L-P	55	6	15	15	7	2	$6.273
B-L-L	55	7	13	16	7	2	$6.258
B-L	55	5	13	18	7	2	$6.231

RBS would save $500,000 during 2000 by limiting the formulary to 3 statins. Decision was based on therapeutic equivalence first, then cost evaluation.

Rheumatoid Arthritis

The Rheumatoid Arthritis Economic Model

- An open Excel spreadsheet that allows comparison of various therapeutic options for the treatment of RA.
- Links intermediate trial-based outcomes (HAQ-DI) to use and cost of health care services (ARMIS)
- Expresses the outcomes in terms of:
  - Incremental health effects - Change in HAQ-DI
  - Incremental costs - Total costs of care
  - Incremental cost-effectiveness - Cost/QALY
- Developed by G. Singh in response to a request from Regence BlueShield.

The Rheumatoid Arthritis Economic Model

- Model Assumptions
  - Calibrated on 13 years of ARAMIS data
  - Links the change in HAQ-DI to changes in resource use, cost and health state preferences adjusting for confounding risk factors.
    - Ex. The mean annual change in costs for patients who progress from a DI score of 2 to 1 is $5,600.
  - Model uses reported changes in DI for treatment group only (not change vs placebo).

The Rheumatoid Arthritis Economic Model

- Output
  - Generates cost/QALY for any compound reporting change in DI and for any annual cost of drug.

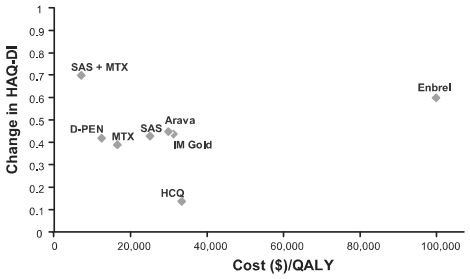
Cost-Effectiveness of Treatments for RA

	Drug Cost Per Year					
	$1,000	$3,000	$6,000	$9,000	$12,000	$15,000
Improvement in DI						
1	**5,000**	**15,000**	**30,000**	**45,000**	**60,000**	**75,000**
0.9	**5,556**	**16,667**	**33,333**	**50,000**	**66,667**	**83,333**
0.8	**6,250**	**18,750**	**37,500**	**56,250**	**75,000**	**93,750**
0.7	**7,143**	**21,429**	**42,857**	**64,286**	**85,714**	107,143
0.6	**8,333**	**24,999**	**50,000**	**75,000**	100,000	125,000
0.5	**10,000**	**30,000**	**60,000**	**90,000**	120,000	150,000
0.4	**12,500**	**37,500**	**75,000**	112,500	150,000	187,500
0.3	**16,667**	**50,000**	100,000	150,000	200,000	250,000
0.2	**25,000**	**75,000**	150,000	225,000	300,000	375,000
0.1	**50,000**	150,000	300,000	450,000	600,000	750,000

** Bolded Numbers Indicate an Acceptable Cost/QALY

Assumes: Straight line depreciation of benefits over 5 year period

Outcomes and Cost-effectiveness of Treatments for Rheumatoid Arthritis



Questions & Answers

AMCP Guidelines: Instructions

- Acquire submission guidelines from health plan
- Confer with plan concerning:
  - Current estimates of disease burden (epi and cost)
  - Current treatment guidelines or pathways
  - Appropriate comparator agents
  - Need for health plan-specific data for modeling (justified)
- Prepare submission in accordance with guidelines
  - Total of 70 pages plus appendices and economic model
- Identify company contact and send completed submission to the health plan

AMCP Guidelines: Implications

- Pharmaceutical Industry
  - Increased responsibility for providing data, particularly economic impact information.
  - Provides the opportunity to establish the value of a new product with evidence
- Health Plan
  - Will evaluate the quality and content of submissions received
  - Will incorporate outcomes and economic evaluation data into formulary consideration

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Necessary Elements for Success

- Support of pharmacy and senior management
- Appropriate training of pharmacy staff
- Format / implementation match stated purpose
- Health plan commitment to making it work
- Experienced and skilled staff or consultants to conduct critical evaluations of submissions
- Establish communication with industry account representatives

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WARNING: **Indiscriminate use of these guidelines may be harmful for some health care systems. The formalized nature and complexity of this process may lend scientific credence to inappropriate decisions or actions. The submission package cannot replace the role of experts in the decision making process.**

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The Role of AMCP

- Develop, publish and refine these guidelines as necessary.
- Support health plan and PBM members and industry on the use of guidelines:
  - Peer-to-peer training of personnel on implementation and effective use
  - Dissemination programs to educate industry and FDA
- Undertake evaluations of the impact of this structured approach on formulary decision making, outcomes and costs.